AMENDMENTS TO THE CLAIMS

Listing of Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

1-36. Cancelled.

37. (Currently Amended) A method of determining ~~the activity of~~ an enzyme's activity or the activity of a G-protein coupled receptor by using mass ~~spectroscopy~~ spectrometry comprising the steps of:

(i) providing a probe having a surface carrying ~~an~~ one or more immobilised enzymes or G-protein coupled receptors;

~~(ii) optionally introducing a test compound;~~

~~(iii)~~(ii) introducing one or more reactants to the immobilised enzymes or to the immobilised G-protein coupled receptors for a time, and in a form sufficient for a reaction to take place;

(~~iv~~iii) drying the probe;

(~~v~~iv) subjecting the probe to mass ~~spectroscopy~~spectrometry;

(~~vi~~v) determining the activity of the enzyme or the G-protein coupled receptor, by detecting the presence and/or absence of one or more products and/or the one or more reactants;

wherein a layer resistant to non-specific protein binding comprising protein repellent molecules is provided on the probe surface, wherein said protein repellent molecules are selected from the group consisting of hydrophilic polymers and self assembled monolayers immobilised on the probe surface and wherein enzyme binding moieties are incorporated into the layer.

38. (Currently Amended) The method of claim 37, wherein said protein repellent molecule is a hydrophilic polymer selected from the group consisting of polyethylene glycol, dextran, polyurethane~~,~~ and polyacrylamide~~, or self-assembled monolayers molecules immobilised on the probe surface.~~

39. (Currently Amended) The method of claim 37, wherein the enzyme is ~~a kinase~~ selected from the group consisting of a serine kinase, a threonine kinase, a tyrosine kinase or a non-protein kinase ~~or~~, an oxidoreductase, a transferase, a hydrolase, a lyase, a ligase, a carboxylase, an esterase, a phosphodiesterase, a protein phosphatase~~, such as a tyrosine phosphatase, a G-protein coupled receptor,~~ an ATP-dependent chaperone, a cyclooxygenase, a cytochrome P450, a sialidase, a short-chain dehydrogenase, a short-chain reductase, and an isomerase.

40. (Currently Amended) The method of claim 37 wherein the one or more immobilised enzymes in step (i) is one or more kinases and step (v) comprises ~~for~~ determining the activity of the one or more kinases by using MALDI mass ~~spectroscopy~~spectrometry.

41. (Previously Presented) The method of claim 40, wherein the one or more reactants comprise a phosphate donor, a phosphate acceptor and a divalent cation.

42. (Previously Presented) The method of claim 41, wherein the phosphate donor is a phosphorylated substrate and the phosphate acceptor is a nucleotide diphosphate (NDP).

43. (Previously Presented) The method of claim 41, wherein the phosphate donor is a nucleotide triphosphate (NTP) and the phosphate acceptor is a substrate to be phosphorylated.

44. (Previously Presented) The method of claim 41, wherein the divalent cation is magnesium or manganese.

45. (Previously Presented) The method of claim 42, wherein the nucleotide diphosphate or triphosphate is an adenine diphosphate or adenine triphosphate.

46. (Previously Presented) The method of claim 37, wherein the detected product is a nucleotide triphosphate or a nucleotide diphosphate.

47. (Previously Presented) The method of claim 46, wherein the nucleotide triphosphate or nucleotide diphosphate are detected as $[NDP]^-$ or $[NTP]^-$ or as one or more adduct peaks thereof.

48. (Previously Presented) The method as claimed in claim 47, wherein the one or more adduct peaks are adduct peaks with a monovalent cation (M^+).

49. (Previously Presented) The method of claim 48, wherein the one or more adduct peaks is selected from the group comprising $[ATPM]^-$, $[ATPM_2]$, $[ATPM_3]$, $[ADPM]^-$, $[ADPM_2]$, and $[ADPM_3]$.

50. (Previously Presented) The method of claim 37, further comprising, between step (iv) and step (v), the step of overlaying the probe with energy absorbing molecules.

51. (Previously Presented) The method of claim 50, wherein said energy absorbing molecules are deposited onto the probe surface in a non-aqueous solvent, followed by evaporation of the solvent.

52. (Previously Presented) The method of claim 37, wherein said probe carries more than one enzyme.

53. (Currently Amended) The method of ~~in~~ claim 37, wherein in step (iii) said one or more reactants are added in the presence of a low salt buffer.

54. (Previously Presented) The method of claim 53, wherein said low salt buffer is a semi-volatile buffer.

55. (Cancelled)

56. (Currently Amended) The method of claim 37, wherein the enzymes are attached to the probe as fusion proteins ~~with~~ via a tag.

57. (Cancelled)

58. (Currently Amended) The method of claim 37, wherein the mass ~~spectroscopy~~ spectrometry is a laser desorption ionisation mass spectrometry~~spectroscopy~~.

59. (Currently Amended) The method of claim 37, wherein the one or more reactants ~~and the optional test compound~~ are introduced to the immobilised enzyme as a droplet~~, such as a droplet having a volume of less than 1 microliter~~.

60. (Withdrawn) A probe for use with a mass spectrometer in the method of claim 37, comprising a support having an electroconductive surface thereon, characterised in that the target surface comprises an array having a plurality of enzymes immobilised thereon, and in that the probe surface is provided with a layer resistant to non-specific protein binding.

61. (Previously Presented) The method of claim 53, wherein said low salt buffer is an ammonium bicarbonate buffer.

62. (Currently Amended) The method of claim 37, wherein said mass ~~spectroscopy~~ spectrometry is a MALDI mass spectrometry.

63. (Currently Amended) A method ~~of determining~~ according to claim 37, wherein a test compound is introduced before, after or with the one or more reactants introduced in step (ii) and the effect ~~a~~ the test compound has on the enzymatic activity ~~of the enzyme,~~ or on the activity of the G-protein coupled receptor is determined by comparison with the results obtained where the test compound is absent. ~~by using mass spectroscopy comprising the steps of:~~

~~(i) providing a probe carrying an immobilised enzyme;~~

~~(ii) introducing a test compound;~~

~~(iii) introducing one or more reactants to the immobilised enzyme for a time, and in a form sufficient for a reaction to take place;~~

~~(iv) drying the probe;~~

~~(v) subjecting the probe to mass spectroscopy;~~

~~(vi) determining the effect the test compound had on the activity of the enzyme, by detecting the presence and/or absence of one or more products and/or the one or more reactants;~~

~~wherein a layer resistant to non specific protein binding comprising protein repellent molecules is provided on the probe surface.~~

64. (Currently Amended) ~~A~~ The method of claim 63 wherein the effect of ~~a~~ the test compound on the activity of one or more kinases using MALDI mass spectrometry is determined.

65. (Currently Amended) ~~A~~ The method of claim 63 wherein the effect of ~~a~~ the test compound on the activity of one or more enzymes using MALDI mass spectrometry is determined wherein the enzyme is selected from the group consisting of a serine kinase, a threonine kinase, a tyrosine kinase, ~~or~~ a non-protein kinase, ~~or~~ an oxidoreductase, a transferase, a hydrolase, a lyase, a ligase, a carboxylase, an esterase, a phosphodiesterase, a protein phosphatase, ~~such as a tyrosine phosphatase, a G-protein coupled receptor,~~ an ATP-dependent chaperone, a cyclooxygenase, a cytochrome P450, a sialidase, a short-chain dehydrogenase, a short-chain reductase, and an isomerase.

66. (New) The method of claim 37 or 63, wherein the reaction of step (ii) is an enzymatic reaction involving co-substrates including NAD, NADP, NADH, NADPH, ATP, GTP, UTP, CTP, UDP-glucose, UDP-glucosamine, UDP-galactose, pyridoxalphosphate, UDP-N-acetyl-D-glucosamine, GDP-D-mannose, dTDP-6-deoxy-L-mannose, GDP-6-deoxy-D-talose, UDP-N-acetylmuramate, (S)-3-hydroxyacyl-CoA, S-adenosyl-L-methionine, acetyl-CoA, L-selenoseryl-tRNAse^{Sec}, (S)-3-hydroxy-3-methylglutarylCoA, 5, 10-methylenetetrahydrofolate, ascorbate, 2-oxoglutarate, glutathione, pyruvate and tetrahydropteridine.